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Ultra-Processed Food and Obesity: The Pitfalls of Extrapolation from Short Studies

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In the short term, eating behavior and body weight may be influenced by many behavioral, psychological, and environmental factors, such as room temperature, social interactions, food appearance, portion size, and more. However, research demonstrates that biology exerts dominant control over body weight, analogous to breathing and fluid balance (albeit over a longer time frame). Whereas many people can lose weight with a low-calorie diet for a few weeks or months, few can maintain significant weight loss despite their best effort. With calorie restriction, hunger increases and metabolic rate slows—homeostatic responses that tend to restore body weight to baseline. The opposite also occurs. With overfeeding, appetite diminishes and metabolism speeds up in the body's attempt to burn off the extra calories (Leibel et al., 1995).

For this reason, we urge caution about extrapolation of short-term data on food intake to obesity prevention and treatment, as in the recent study by Hall et al. (2019) on ultra-processed food.

On first pass, the primary findings of this 2-week study do not surprise us. Confine U.S. volunteers interested in a food study to a metabolic ward, give them unlimited access to processed foods that appeal to the American palate, allow them to eat as much of them as they like, and some will overeat. The critical questions are: What is driving food intake? Does this effect have relevance to the chronic control of body weight? We would like to make two main points.

Diet composition. On the "ultra-processed" versus "unprocessed" diet, participants ate substantially more total carbohydrate, added sugar, saturated fat, and sodium, and less protein, polyunsaturated fat, and soluble fiber. Non-beverage energy density was 85% higher on the ultra-processed diet. Moreover, at 45 g per day, the unprocessed diet had almost triple the intrinsic fiber of an average Western diet. Each of these factors, previously linked to food intake or metabolism, may have influenced the study findings independently of food processing.

Although an increase in non-beverage energy density of about 30% (less than half that in the current study) (Bell et al., 1998) resulted in a change in food intake of similar magnitude as that reported by Hall et al., long-term trials did not show a sustained effect (Saquib et al., 2008). Indeed, low-fat diets, despite their inherently lower energy density, are inferior to all higher-fat diet comparisons in meta-analyses of weight loss trials (Tobias et al., 2015). Perhaps for this reason, food intake on the ultra-processed, energy-dense diet decreased significantly over time ($p < 0.0001$), raising the possibility that the observed effects may be previously recognized and transient.

Other aspects of the ultra-processed diet might drive long-term weight gain through biological mechanisms also largely independent of food processing, including the higher carbohydrate-to-protein ratio and greater added sugar content, resulting in an increased glycemic load (Ludwig and Ebbeling, 2018). In Diogenes, the largest macronutrient-controlled trial to date, sequential increases in glycemic load led to progressively greater weight gain over 6 months (Larsen et al., 2010).

The differences in macronutrients and sugar could also influence metabolism (St-Onge et al., 2004). The present study, in which energy expenditure did not differ by diet, was not designed to see such an effect, as participants were in a dynamic stage of weight change, potentially masking metabolic compensation.

Processing. Beyond concerns about extrapolation of short-term data, the study's implicit aim to end the "perpetual diet wars"—between proponents of low-fat and low-carbohydrate diets, or between vegans and "Paleo" adherents—may raise additional questions. One could design a highly processed meal with Beyond Burger (a newly popular meat substitute containing 21 refined ingredients), vegan cheese substitute (containing a dozen refined ingredients), vegetables cooked in refined (but high-polyunsaturated) vegetable oil, and an artificially sweetened (sugar-free) beverage, or an isocaloric, minimally processed meal of dry chicken breast, baked potato, and fat-free milk heavily sweetened with raw honey. Although these meals differ markedly in processing, adversaries on several fronts of the "diet wars" might still find grounds for disagreement.

In fact, many of the foods utilized on the ultra-processed diet (e.g., breads, baked potato chips, and apple sauce) and various refined grain products are, from a food science perspective, no more extensively processed than olive oil, dark chocolate, or nut butters. The processing of olives to olive oil removes virtually all the fiber and fully disrupts the natural food structure. Dark chocolate typically contains a half-dozen or more refined ingredients. However, most of the aforementioned high-carbohydrate foods (e.g., white bread and potato chips) consistently top the list for weight gain in prospective studies (Mozaffarian et al., 2011), whereas these high-fat foods (e.g., olive oil) have the opposite effect. Furthermore, the study cannot tell us whether freshly baked bread, potato chips made from three natural ingredients, or applesauce made from two ingredients—each explicitly not ultra-processed (Monteiro et al., 2018)—would have any different effects than the varieties used instead.

Thus, an understanding of the mechanisms by which ultra-processed foods may influence energy intake and adiposity is critical to solving the obesity epidemic. Carbohydrate processing accelerates the rate of digestion and subsequent post-prandial glycemia and insulinemia, responses mechanistically linked to weight gain (Ludwig and Ebbeling, 2018). By contrast, the extent of processing has no comparable effect on high-protein and high-fat foods.

The concept of ultra-processing (Monteiro et al., 2018) provides a useful system to identify industrial products with the worst of numerous nutritional qualities; substantial evidence links this dietary pattern with obesity and chronic diseases. However, the findings of Hall et al. may be transient and independent of processing per se. It might be tempting to attribute modern-day diet problems predominantly to food processing, thus implicitly shifting responsibility for the obesity epidemic to the food industry. But knowledge of the chronic drivers of food intake, including the metabolic effects of food independent of calorie content, is needed to mitigate the risks of misguiding the food industry in how to formulate more healthful food products, and the public in nutrition recommendations, as previously occurred during the low-fat diet era. Although data on the acute control of food intake can be useful, long-term studies will be needed to resolve these controversies.

DECLARATION OF INTERESTS

D.S.L. received royalties for books on obesity and nutrition that recommend a reduced glycemic load diet. A.A. is recipient of honoraria as speaker for a wide range of Danish and international concerns, and receives royalties from popular diet and cookery books on low glycemic load and personalized diets. S.B.H. is a member of the Medifast Medical Advisory Board. W.C.W. received royalties for books on nutrition and obesity. The other authors have no disclosures. This work was done without financial sponsorship.

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